Finite element-based fast force recovery for 2.5D Traction Force Microscopy experiments

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The quantification of cellular forces provides insight on the way cells sense and react to the extracellular matrix (ECM) in a variety of physiological and pathological processes. Traction Force Microscopy (TFM) is commonly used to estimate these forces from the displacement of fluorescent beads embedded in a gel that mimics the ECM mechanical properties. Recent so-called 2.5D TFM studies have revealed the importance of normal forces exerted by cells lying on 2D gels, emphasizing the 3D nature of cell forces.
The Finite Element Method (FEM) can be used to recover 3D traction forces by generating an invertible stiffness matrix. The stiffness matrix can be built from a number of Green functions obtained by applying unit tractions in each Cartesian direction to each facet in the surface of the meshed substrate and solving the forward problem for the stress equilibrium [1]. However, the large volumetric grids (~10,000 elements in the surface) required to get acceptable values of sensitivity resolution affect the computational efficiency, which, ultimately, can limit the applicability of FEM-based solutions to large experimental data sets.
Here, we present an alternative FEM-based methodology for 2.5D TFM experiments to generate the stiffness matrix in an efficient and flexible way.

Assuming the cell is located far enough from the lateral boundaries of the substrate, the Green function only depends on relative displacements of the spatial points and not on the absolute location of the applied unit tractions, i.e. it can be considered shift-invariant. Therefore, we can build the stiffness matrix from a single Green function (per Cartesian direction) and a number of shifted copies of it, instead of calculating the Green function for every node on the substrate surface.
Abaqus CAE 6.12 was used to mesh the substrate and apply a unit traction at the center of its top surface. The resulting Green function was adaptively sampled (finer mesh closer to the force application point) to allow a subsequent interpolation step in Matlab, which allows reusing the same Green function for different data sets as long as the mechanical properties of the material remain unaltered.

Our results show similar resolutions and sensitivities than previous methodologies [1] with a dramatic improvement in the computational time, which allows a fast recalculation of the stiffness matrix for TFM studies under different mechanical conditions. Our method holds great promise for cases where computational speed is key, such as for nonlinear materials.

Reference

[1] Legant W R, Choi C K, Miller J S, Shao L, Gao L, Betzig E and Chen C S 2013 Multidimensional traction force microscopy reveals out-of-plane rotational moments about focal adhesions *Proc. Natl Acad. Sci. USA* **110** 881–6

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